I. Remarks

Claims 128, 131, 135-137, 147-148, and 151-155 are pending in the application. Claims 129-130, 146, and 156-157 are canceled herein. A Request for Continued Examination along with the requisite fee accompanies this Submission. Note that this application USSN 10/10/066,831 is now assigned to Zivena, Inc. Zivena is the legal owner of the parent of this application, as well as, all of the sister cases listed in Table I below.

Table 1.

Docket No.	Serial No.	Filing Date	Title	PATENT No.
22,000(1)	60/033,789 Provisional	12/30/1196	Formulation and Method for Treating Neoplasms by Inhalation	Expired
22,000(1)	09/000,775	12/30/1997	Formulation and Method for Treating Neoplasms by Inhalation	6,471,943
22000(1)CON1	09/875,677	06/06/2001	Formulation and Method for Treating Neoplasms by Inhalation	6,419,901
22000(1)CON2	09/875,680	06/06/2001	Formulation and Method for Treating Neoplasms by Inhalation	6,348,209
22000(1)CON	09/875,345	06/06/2001	Formulation and Method for Treating Neoplasms by Inhalation	6,419,900
22000(1)9711-1	09/517,915	03/03/2000	Formulation and Method for Treating Neoplasms by Inhalation	6,451,784

By telephone call dated November 19, 2004, Examiner Alton Pryor indicated the following:

1. The Docketing Group did not enter Applicants' Response After Final dated October 10, 2004 because it was not signed; and
2. An additional fee of $54.00 is due in the case for additional claims.

A true duplicate of the Response dated October 10, 2004 signed by Patricia A. Coburn, attorney of record in the above-identified application was faxed to the USPTO on 11/20/2004.

Applicants have reviewed the file of the above-identified application and according to our records, no additional fees are due for claims pending in this application. Table 2 summarizes the fees paid for the claims in the above-identified application.

Table 2.

Summary of Claims Paid For in Application

FORM	DATED	TOTAL CLAIMS	NO. OF INDEPENDENT CLAIMS	EXCESS CLAIMS PAID FOR	METHOD OF PAYMENT	LARGE/ SMALL ENTITY CLAIMED
PTO/SB/17 (11-01)	02-04-2002	23	1	3 Dependent	Credit Card charge	Large
PTO/SB/17 (05-03)	07-01-2003	24	2	1 Dependent	Credit Card charge	Small
PTO/SB/17 (11-03)	01-28-2004	17	1	None	Check	Small
PTO/SB/17 (10-04v2)	10-11-2004	12	1	None	Check	Small

Based on the records summarized above, Applicants do not believe that any additional fees are due in the above-identified application. However, if Applicants are in error, the USPTO is respectfully requested to provide detail of the fee that is due and Applicants will promptly pay such amount.

II. Rejection under 35 USC 102(e)/103(a)

Examiner has rejected Claims 128-130, 135-136, and 150 under 35 USC 102(e) as being anticipated by Kaufman. Examiner relies on Claims 11 and 12 of Kaufman as well as the abstract to assert that:

> "Kaufman clearly states that his drug composition can be delivered to the lungs as a breathable (inhalation) gas (aerosol)."

To facilitate the discussion that follows, Claims 11 and 12 of Kaufman and Claim 128 of the above-identified invention are compared in below.

Kaufman	USSN 10/066,831
11. A method of delivering a drug to the lung of an animal comprising the step of: administering a stable homogeneous, water-in-perfluorochemical liquid dispersion to the animal lung or a section thereof, said dispersion comprising a perfluorochemical liquid, water, surfactant and drug, said perfluorochemical constituting greater than 50% by volume of said dispersion, said drug contained in said dispersion in an effective therapeutic amount.	128. A method of treating cancer of the respiratory tract in a patient in need of treatment which comprises administering by inhalation a pharmaceutically safe and effective amount of an aerosolized vesicant agent; wherein said vesicant anti-cancer agent is unencapsulated and wherein the particle size of said aerosol is from about 0.1 μm to about 10.0 μm.
12. The method of claim 11 further comprising the step of delivering a breathable gas to the lung with a mechanical ventilator during said administration.	

As can be clearly seen when Claim 11 of Kaufman is compared to Claim 128 of the present invention, the method taught by Kaufman is unequivocally different from the method claimed herein. Kaufman does not deliver a drug to the lungs of a patient in the form of an aerosol. Kaufman teaches the "administration" of a water-in-perfluorocarbon liquid dispersion directly to the lungs. The liquid dispersion is placed in the lung (i.e. administered) using an endotracheal tube. In contrast to the method of Kaufman, in the practice of the method claimed herein, an aerosol of fine droplets containing the drug is inhaled into the lungs by the patient being treated.

Claim 12 of Kaufman provides that a "breathable gas" may be administered to the lung of a patient using a mechanical ventilator in addition to the administration of the liquid perflurocarbon dispersion. The breathable gas referred to by Kaufman is air or oxygen and is administered to the patient using a conventional gas ventilator.

As would be recognized by one skilled in this art, Kaufman describes a method known as liquid ventilation or partial liquid ventilation (PLV). A brief discussion of the history of liquid ventilation can be found at the Alliance Pharmaceutical website at (www.allp.com/LiquiVent). Alliance manufactures the only FDA approved perfluorocarbon which is sold under the tradename LiquidVent® (sterile perflubron). The website teaches the following.

> "A breakthrough occurred in 1991, when it was discovered that liquid ventilation could be performed effectively in normal pigs without the use of a liquid ventilator. Sustained, highly efficient gas exchange was achieved by simply filling the lung with a PFC to a prescribed level (Claim 11 of Kaufman), and then reconnecting the conventional gas ventilator (Claim 12 of Kaufman). This discovery ... established the feasibility of a simplified, practical method of liquid ventilation ...[T]he PLV technique has ... been shown to produce significant improvements in lung function and viability in numerous animal studies of diseased or injured lungs. By opening closed alveoli and keeping them open with lower ventilator pressures and reduced oxygen settings, and by increasing the flow of blood to the more open portions of the lung, selected PFCs can apparently minimize lung damage and enable earlier cessation of ventilator therapy."

Kaufman's invention is to new, stable reverse micellar water-in-perfluorochemical (WIP) liquid dispersions and the use of such liquid dispersions in liquid ventilation and partial liquid ventilation. Col.3, lines 18-21.

Kaufman specifically teaches that:

> ... delivery of ... therapeutic agents by this method is an enormous improvement over current techniques, since the active agent is uniformly distributed across the entirety of the alveolar space, making it available to the distant small alveolar beds which are not accessible by nebulization or aerosol technologies. Col 3, lines 1-6.

In discussing the benefits of liquid ventilation using the WIP dispersions of the invention in the treatment of cystic fibrosis, Kaufman reports that the then current treatment of choice is administration of rDNAse twice per day via a metered dose inhaler. Kaufman goes on to say that "... if the lungs could be completely lavaged with the rDNAse one might be able to reduce the number of treatments by an order of magnitude. See Col 4, lines 26-52. Clearly, Kaufman believes that liquid lavage using the WIP dispersions is superior to administration of rDNAse as an aerosol using a metered dose inhaler.

Examiner's attention is directed to Col 8, lines 15-67 and Col 9, lines 1-4 where the protocol used to test various WIP liquid formulations of the Kaufman invention in liquid breathing is described in detail. Specifically, at Col 8, lines 52-58, the references teaches that the rodent is disconnected from the rodent ventilator, the WIP dispersion (liquid) is instilled into the lungs via the endotracheal tube, and then the animal is reconnected to the ventilator. The WIP liquid fills the lungs to the functional residual capacity volume (30 ml/kg).

In the practice of the method claimed herein the vesicant anticancer agent is either dissolved or suspended in a liquid or gas or mixed with the pharmaceutically acceptable excipients used to prepare a dry powder and then aerosolized to produce aerosol particles from about 0.1 μm to about 10.0 μm. The aerosol is produced using conventional aerosolization means known in the art, i.e., a nebulizer, inhaler, metered dose inhaler or electrostatic

aerosolization means. The patient inhales the aerosol droplets into her lungs when practicing the method of the invention claimed herein. In contrast, in the practice of the method described by Kaufman. a nurse, doctor or respiratory therapist must place the PFC dispersions into the lungs of the patients using an endotracheal tube.

Kaufman does not anticipate Applicants' claimed method within the meaning of 35 USC §102(e) because as discussed herein, Kaufman describes an entirely different method. Kaufman specifically teaches aerosols containing drugs are different from the WIP liquid dispersions developed by Kaufman. See Col 3, lines 1-6.

Kaufman does teach that Adriamycin® (doxorubicin HCl) may be delivered to the lungs as part of a WIP liquid dispersion. However, there is nothing in Kaufman that suggests that administration of a drug to the lungs using liquid ventilation or partial liquid ventilation methodology is the same as a method for administering doxorubicin as an aerosol to the lungs of a patient via inhalation of the aerosol.

Until the work of Applicants which led to the filing of USSN 000,775 (now US Pat 6,471,943), the parent of the above-identified application, there was no teaching or suggestion in the art that an anticancer drug which is a vesicant could be aerosolized and safely inhaled by the patient being treated.

Applicants thoroughly discussed the reasons why one skilled in this art would not find the presently claimed method obvious in view of Kaufman. In fact, Applicants offered evidence in the form of copies of Rule 132 Declarations filed in USSN 09/000,775 the parent of this application. Examiner offers no evidence that counters any of the evidence or arguments presented by Applicants in the Response filed 12/18/2003, instead Examiner dismisses Applicants arguments and evidence and argues that "Kaufman clearly states that his drug composition can be delivered to the lungs as a breathable (inhalation) gas (aerosol). It is respectfully asserted that as discussed above, Kaufman clearly does not state any such thing.

Based on the evidence and arguments presented in Applicants Response filed 12/18/2003 and the arguments presented herein, Applicants respectfully assert that they have presented sufficient evidence and arguments to shift the burden to Examiner to provide concrete evidence , not merely assertion, that Applicants analysis of the teachings of Kaufman is incorrect; absent such evidence, it is respectfully asserted that Examiner's rejections of the claims as amended under 35 USC §102(e)/103(a) have been overcome.

III. Statutory Double Patenting Rejection

Examiner rejects Applicants' claims for double patenting over two of Applicants' issued patents: US 6,384,209 and US 6,419,901. Statutory Double Patenting or "same invention" type double patenting, prevents an inventor from obtaining more than one valid patent covering the same invention. This prohibition is rooted in Section 101 of the Patent Code, which provides that an inventor "may obtain *a* patent" (emphasis added) for a new invention. The word "a" in this provision has been interpreted to mean only one patent may issue for each distinct scientific advance. *In re Vogel*, 422 F.2d 438, 441, 164 USPQ 619, 621 (C.C.P.A. 1970). The court in Vogel stated that the test for same invention double patenting was whether the two different patents covered "identical subject matter."

When Claim 128 the broadest claim in this application is compared to Claim 1 of the '209 patent and claim 1 of the '901 patent it is clear that Claim 128 is broader in scope than either of first claims of the patents. Claim 128 claims the use of all vesicant anticancer agents in the method of the invention. Claim I of the '209 patent is limited to a specific type of vesicant anticancer agents, i.e., the vinca alkaloids. Likewise, Claim 1 of the '901 patent is directed to the anthracycline vesicant anticancer agents.

When Claims 131,135,136,137, and 147-149 are compared to the claims of the '209 and '901 patents using the "identical subject matter" test it is clear that these claims are not identical to any of the claims of the patent.

MPEP Section 804.02 states that a rejection based on the statutory type of double patenting can be avoided by canceling the conflicting claims in all but one of the pending application(s) or patent, or by amending the conflicting claims so that they are not coextensive in scope. A terminal disclaimer is not effective in overcoming a statutory double patenting rejection. It is respectfully asserted that Applicants claims as amended are not coextensive in scope with any of the claims of US 6,384,209 and US 6,419,901 and thus the statutory double patenting rejection has been overcome.

Based on the amendments to the claims made herein and on the analysis presented hereinabove it is respectfully asserted that the Statutory Double Patenting rejection has been overcome and should be with drawn.

IV. Conclusion

Based on the amendments and arguments made herein, it is respectfully asserted that all of Examiner's objections and rejections have been overcome and that this application is in condition for allowance. Examiner is respectfully requested to withdraw all rejections and to issue a Notice of Allowance.

Respectfully submitted,

Dated: December 16, 2004

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